

REMARKS/ARGUMENTS

Claims 1-25 are pending. Claims 13-25 stand withdrawn. Claim 1 has been amended to more distinctly claim what Applicants regard as their invention. No new matter has been introduced by way of the amendment to claim 1.

I. *The rejections under 35 U.S.C. § 103(a) should be withdrawn*

Claims 1-5 and 7 stand rejected as being unpatentable over Diksic *et al.* (*Int. J. Nucl. Med. Biol.* 9: 283-285 (1982)) in view of Suzuki *et al.* (EP0282703B1) and Shiba *et al.* (US 4,458,302) and further in view of Kihlberg *et al.* (US2004/0197257A1).

Increasing the specific activity (SA) of PET tracers is imperative from toxicological, biochemical, and regulatory perspectives. [¹¹C]Phosgene is an important labelled building block for the production of [¹¹C-carbonyl]ureas and carbamates, both cyclic and acyclic. Though established over 30 years ago, its synthesis is still evolving, with the focus on improving specific radioactivity and the stability of production.

Applicants designed a system and developed the claimed method, which uses the system, for the batch-wise generation of [¹¹C]phosgene. The claimed method not only reduces reaction volumes and associated amounts of reactants, but it also produces [¹¹C]phosgene with a decay-corrected radiochemical yield of 70–85% and a surprisingly high radioactivity of 200 GBq/μmol, which amounts to 200 TBq/mmol. In addition, the claimed method significantly reduces isotopic dilution during the labelling synthesis to the point that it becomes negligible. These data and findings were presented by two of the named inventors, Oleksiy Itsenko and Tor Kihlberg, on September 10, 2010 at the 2010 World Molecular Imaging Congress in Kyoto, Japan. A copy of the poster and an abstract, are provided herewith.

The claimed method, by virtue of the fact that it generates [¹¹C]phosgene batch-wise when the Cl₂ gas and the ¹¹CO are introduced into the reaction chamber and irradiated therein, produces [¹¹C]phosgene with a surprisingly and unexpectedly high specific activity. The high specific activity of the [¹¹C]phosgene generated by the claimed method is a necessary result of how the method is conducted. Applicants submit that one of skill in the art could not have achieved such high specific activity using a continuous-flow system such

as Diksic's. Diksic's "on-line" method, where ^{11}CO and Cl_2 are u.v.-irradiated as the gases flow through a quartz spiral (i.e., in a continuous-flow mode), produces $[^{11}\text{C}]$ phosgene with a specific activity that is about **135 times less** than the specific activity of the $[^{11}\text{C}]$ phosgene produced via the claimed method. Diksic, in fact, appears puzzled as to why the specific activity of his $[^{11}\text{C}]$ phosgene was so low. Diksic posits that the low specific activity of the $[^{11}\text{C}]$ phosgene can somehow be traced to the chlorine gas used. Diksic at 284, right-hand column ("The specific activity of our $^{11}\text{COCl}_2$ measured by diphenylurea¹ is about 1.48 TBq/mmol (40 Ci/mmol), 10^5 times lower than the theoretical specific activity of $^{11}\text{COCl}_2$. We suspect chlorine, even though we have used research purity chlorine (99.95%), since the specific activity of $[^{11}\text{C}]$ phosgene is at least 2.5×10^3 times lower than the specific activity of $[^{11}\text{C}]$ carbon monoxide.").

Applicants submit that Suzuki, Shiba or Kihlberg do not remedy the significant deficiencies in Diksic. Accordingly, Applicants submit that the claimed method is not obvious in view of the teachings of Diksic alone or even in combination with Suzuki, Shiba, and/or Kihlberg. Resonsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1-12 stand rejected as being unpatentable over Kihlberg *et al.* (U.S. Patent 7,521,544B2) in view of Diksic *et al.* Applicants respectfully disagree.

As an initial matter, Applicants submit that 35 U.S.C. § 103(c) provides that subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of 35 U.S.C. § 102, shall not preclude patentability under 35 U.S.C. § 103(c) where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.

The earliest effective filing date for the instant application is December 3, 2003, which is the date on which Appl. Ser. No. 60/526,720 was filed. The earliest effective filing date for the '544 Kihlberg patent is October 31, 2003. But, the '544 Kihlberg patent was not published as WO2005/042441 until May 12, 2005. Accordingly, the '544 Kihlberg patent appears to qualify as prior art under of 35 U.S.C. § 102(e), since it has an earlier effective

¹ Applicants use the same diphenylurea method to quantitate the specific activity of the $[^{11}\text{C}]$ phosgene produced by the claimed method.

filing date, but a publication date that is after the earliest effective filing date of the instant application.

The '544 Kihlberg patent and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person. Accordingly, under 35 U.S.C. § 103(c), the '544 Kihlberg patent alone or in combination with any of the references cited, shall not preclude patentability of the instant claims. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) with regard to the '544 Kihlberg patent in view of Diksic are therefore respectfully requested.

II. *The Obviousness-Type Double Patenting Rejection Should Be Held in Abeyance*

Claims 1-7 stand rejected under the judicially-created doctrine of obviousness-type double patenting (ODP) as being unpatentable over claims 1-7 of U.S. Patent No. 7,521,544 in view of Diksic. Claims 8-12 stand provisionally rejected under ODP as being unpatentable over claims 8-11 of co-pending Appl. Ser. No. 12/423,034.

While not acquiescing to the propriety of any of the ODP rejections enumerated above, Applicants respectfully submit that once the claims of the instant application are held to be otherwise allowable, Applicants will consider filing a duly executed terminal disclaimer to overcome the ODP rejections. In the meantime, Applicants respectfully request that all of the ODP rejections be held in abeyance.

Applicants conclude, on the basis of the above argumentation, that the pending claims are patentable and requests favorable consideration.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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